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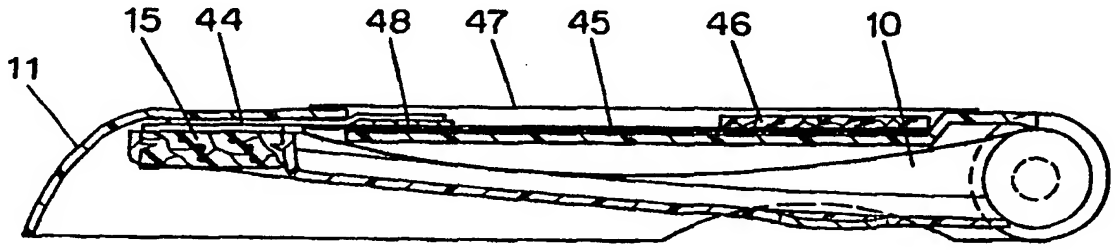
(54) Title: DEVICE FOR DETECTION OF A SUBSTANCE IN A LIQUID SAMPLE



(57) Abstract

A foldable test device for detection of an analyte in a liquid sample, for example for detection of hCG in urine as a pregnancy test, has two housing members (10, 11) connected by a hinge (12). The hinge (12) permits movement between an open position in which the two housing members (10, 11) are disposed substantially linearly, and a folded position in which the free end of the first housing member and the free end of the second housing member are disposed in proximity to one another. A sample–absorbing member (15) is disposed at the free end of first housing member (10), and a chromatographic test element (45, 48) responsive to a target substance is disposed on the second housing member. Sample liquid is collected in the sample–absorbing member (15) with the device in the open position. The device in then folded to bring the sample–absorbing member (15) into contact, directly or indirectly, with the chromatographic test element (45, 48) such that the liquid is transferred to the chromatographic test element (45, 48).

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DEVICE FOR DETECTION OF A SUBSTANCE IN A LIQUID SAMPLE

DESCRIPTION

Background of the Invention

This application relates to a device for detection of a substance in a liquid sample, and particularly to a device which is useful for performing tests on urine specimens to determine pregnancy.

Test devices are known in a variety of formats for testing liquid biological samples, including blood, urine and saliva for the presence of an analyte. Many of these devices include immunoreactive materials (i.e., antibodies or antigens) which react with the analyte to produce a detectable response. Such devices are particularly common among the over-the-counter pregnancy tests.

For use in the over-the-counter market, it is desirable to make the process of performing the test as simple and as unobjectionable as possible. Thus, for example, it is desirable to reduce or eliminate the number of sample mixing steps which a user has to perform, as well as to reduce the potential for the user to come into contact with the sample. For aesthetic and hygienic reasons, this latter is particularly true where the sample is urine.

European Patent Application No. 291 194 discloses an analytical test device which can be used for pregnancy testing. The device has a hollow casing which encloses a dry porous carrier on which test reagents are applied. The dry porous carrier is in contact with a bibulous sample receiving member which extends outside the housing. A liquid sample such as urine is applied to the sample receiving member and permeates through the sample receiving member to reach the porous carrier where it interacts with the test reagents. When not in use, the protruding bibulous member may be covered by a removable cap. A similar device is disclosed in European Patent Application No. 653 638 which the removable cap can be placed over the bibulous member or over the opposite end of the device.

These devices are simple to use, but are not without drawbacks. For example, because the cap is removable, it may be separated from the remainder of the device and lost. In this case, the protruding urine soaked bibulous member would remain exposed, posing a potential sanitary risk. Also, the distance between the urine collection point and the window in which the result is displayed is very short, making it possible to splash urine on the

window. Urine entering through the result-display window invalidates the test, because the flow of material is reversed.

Another known pregnancy test device having a structure similar to that described in EP 653 638 is sold by Parke Davis under the trade name "e.p.t. pregnancy test.". In this device, the removable cap is replaced by an open-ended sliding cover, which is moveable between a storage position in which the cover surrounds the sample receiving member, and a collection position in which the slidable cover to drawn back over the center of the housing to expose the sample collection member. This design overcomes the problem of losing the cap because the slidable cover is not easily removed from the housing part of the device, but because of the large open-end of the slidable cover it still poses some risk of contamination or sanitary issues because urine-soaked sample collection member remains partially exposed. Furthermore, there is a risk that the user's fingers will come in contact with the urine-soaked sample collection member when sliding the cover closed.

JP 7120467 discloses a test device having a cover which pivots between a position covering a urine-collection wick that extends from the main part of the holder and a position at the opposite end of the holder. This device is all one piece, but does not really isolate the urine-soaked wick after use.

It is an object of the present invention to provide a device for detection of a substance in a liquid sample, particularly as pregnancy test device, which overcomes these drawbacks.

It is a further object of the present invention to provide a test device, particularly a pregnancy test device, in which the sample collection member is contained within the main housing of the device both before and after sample collection.

Summary of the Invention

In accordance with the present invention, these and other objects are achieved using a foldable device having two housing members connected by a hinge. The hinge permits movement between an open position in which the two housing members are disposed substantially linearly, and a folded position in which the free end of the first housing member and the free end of the second housing member are disposed in proximity to one another. A sample collection member comprising at least a sample-absorbing member is disposed at the

free end of first housing member, and a chromatographic test element responsive to a target substance is disposed on the second housing member. Sample liquid is collected in the sample-absorbing member with the device in the open position. The device is then folded to bring the sample-absorbing member into contact, directly or indirectly, with the chromatographic test element such that the liquid is transferred to the chromatographic test element.

Brief Description of the Drawings

Fig. 1 shows an exterior side view of a device in accordance with the invention in the open position;

Fig. 2 shows an exterior side view of a device in accordance with the invention in the folded position;

Fig. 3 shows a top view of a device in accordance with the invention;

Figs. 4A and 4B show longitudinal cross-sections through the device of Fig. 3;

Figs. 5A and B show transverse cross-sections through the device of Fig. 3 along section lines CD-CD; and

Fig. 6 shows a cross section of the assembled device in the folded position.

Detailed Description of the Invention

The present invention provides a foldable device for the detection of a target analyte in a liquid sample. Figs. 1 and 2 show the device of the present invention when viewed from the side in open and folded positions, respectively. As shown, the device comprises a first housing member 10 which is pivotably connected to a second housing member 11 by a central hinge member 12. In the open position as shown in Fig. 1, the first and second housing members 10, 11 are substantially linear. Sample is collected at the free end 15 of the first housing member 10 when the device is in the open position. In the folded position as shown in Fig. 2, the first housing member 10 is received within the second housing member 11. A notch 14 in the second housing member 11 may be provided to facilitate unfolding the device from the folded to the open position. The latter is especially appropriate where the device is provided initially in a folded configuration to permit packaging in a minimum volume, and must be unfolded prior to use.

Fig. 3 shows a top view of a device in accordance with the invention. The first housing member 10 has a textured press-pad 31 which can be used to press the first housing member 10 into the folded position. Second housing member 11 has a similar press-pad 32 which is used to provide a firm grip on the device when it is in the open position. Second housing member 11 also has a window 33 for viewing of test results on a chromatographic test element disposed within the second housing member. The device may also include a depression 34 for receiving a label. The label 34 may extend over the window 33, in which case at least a portion of the label is formed from transparent material.

Figs 4A and 4B show cross-sections of the first and second housing members of the device of Fig. 3 along section line B-B. As shown in Fig. 4A, the first housing member 10 may be formed as a solid rod 41, A T-shaped member, or a U-shaped member without internal structure extending to the urine collection member 15 at the free end of the first housing member.

In contrast, the second housing member 11 has a fairly complicated structure when viewed in cross-section as shown in Fig. 4B. The second housing member has an end portion 42 and a support portion 43 which are separated by a gap through which a liquid transfer member 44 extends. The liquid transfer member 44 is in contact with a chromatographic test strip 45 and a reagent pad 48 which are disposed on the support portion 43 of the second housing member 11 so as to be visible through window 33. An upstream absorbent pad 46 is also disposed on the support portion 43, and the chromatographic test strip 45, the reagent pad 48 and the upstream absorbent pad 46 are covered by a transparent cover 47.

The first and second housing member are pivotably joined together to permit movement between an open and a closed position as shown in Figs. 1 and 2. This joining can be accomplished in any manner which provides the desired degree of flexibility. One embodiment of a preferred approach is illustrated in Figs. 5A and B which show transverse cross section through the device of Fig. 3 along section lines CD-CD. Fig. 5A shows the section looking towards the first housing member 10. The first housing member 10 has an inverted-U-shaped configuration, with two protrusions 12 disposed on the exterior surfaces which are centered on a common axis of rotation. The protrusions 12 interact with openings 51 in the second housing member 11 (Fig. 5B) to create a hinged joint. Variations of this

design can also be employed, including the use of depressions in place of the openings 51 and the use of protrusions on the interior surface of second housing member which interact with openings or depressions in the exterior surface of the first housing member.

Fig. 6 shows a cross section of the assembled device in the folded position. In the folded position, the sample-absorbing member 15 of the sample collection member is pressed into contact with the liquid transfer member 44. Liquid collected in the sample-absorbing member 15 wicks into the liquid transfer pad 44 and then into the chromatographic test element formed from chromatographic test strip 45 and reagent pad 48 to produce a test result which is detectable through transparent cover 47.

The device of the present invention can be used to detect a wide variety of analytes in a liquid sample, but is particularly suited for the detection of immunoreactive analytes in urine. A preferred application of the device is as a pregnancy test stick, in which case the chromatographic test strip is specific to an indicator of pregnancy, for example human chorionic gonadotropin (hCG).

To prepare a device for use as a pregnancy test stick, the chromatographic test strip is suitably a plastic-backed nitrocellulose strip treated with two physically-discrete reactive regions. The first reactive region is a test region comprising a monoclonal antibody, for example a mouse monoclonal antibody, directed to an epitope of hCG. The second reactive region is a control region comprising a polyclonal antibody which binds to a non-human immunoglobulin. For example, the control region can suitably be formed from an affinity-purified fraction of goat antibody to mouse IgG. The control region binds to the antibody from the first reactive region, whether or not hCG (the target substance) is present.

This chromatographic test strip is utilized in contact with a reagent pad which contains a detectably-labeled antibody specific to a different epitope of hCG. For example, the reagent pad can be a rayon pad which has been saturated with gold particles coated with a mouse anti-hCG monoclonal antibody and dried. These particles are suitably applied in a buffer which will facilitate the stability and remobilization of the gold particles, such as a buffer containing TAPS buffer salts, bovine serum albumin, Triton X-100, Sweet 36 corn syrup solids and sodium azide.

The reagent pad is disposed in contact with a liquid transfer member. The liquid transfer member may be made from absorbent paper, for example Ahlstrom 939 paper,

and is preferably pretreated with Triton X-100 in TAPS buffer (pH 8.0) to reduce non-specific interactions of gold particles with the test region on the chromatographic test element.

In use, sample liquid is transferred from the sample-absorbing member located at the free end of the first housing member to the liquid transfer member. The sample liquid then passes through the reagent pad, remobilizing the detectably-labeled anti-hCG antibodies and causing them to migrate into and through the chromatographic test strip. These labeled antibodies will react with the control region to produce a colored region on the test strip regardless of the content of the sample. The labeled antibodies will only bind to the test region, however, when hCG is present, since binding occurs through the formation of a labeled antibody-hCG-immobilized antibody sandwich.

Specific antibodies which can be used in making a pregnancy test device in accordance with the invention are well-known in the art, having been used in other chromatographic pregnancy test devices. Exemplary antibodies are disclosed in US Patent No. 5,602,040, US Patent No. 5,611,995, US Patent No. 4,313,734 and European Patent No. 291 194, which are incorporated herein by reference.

In a preferred embodiment of the invention, an upstream absorbent material, such as upstream absorbent pad 46 in Fig. 4B is included in the device. This upstream absorbent material receives liquid which has passed through the chromatographic test strip and acts as a sink to both draw liquid through the test strip and to prevent reverse flow of liquid in the assay strip. A suitable material for use as an upstream absorbent pad as shown in Fig. 4B is Ahlstrom 901 paper.

The liquid collection member which is disposed at the free end of the first housing member must include at least a sample-absorbing member which can transfer liquid to the liquid transfer member when the device is in the folded position. The sample-absorbing member can be in the form of a flat pad or absorbent material, or it may have a textured or grooved surface. The sample-absorbing member may be made from a variety of absorbent materials including cellulose acetate, polyethylene, polypropylene and ethylene vinyl acetate wick materials. Materials of this type are available from American Filtrona Corp. and from Porex Technologies. Polyethylene and ethylene vinylacetate wick materials

can be molded into specific sizes and shapes which facilitates attachment of the sample-absorbing member to the free end of the first housing member.

The sample-absorbing member may also take other forms besides an absorbent pad. For example the sample-absorbing member may be a molded plastic piece having straight or conical capillary channels formed therein which catch urine and allow it to spread outwards when placed in contact with the liquid transfer member. The sample-absorbing member may also be a brush similar in structure to a toothbrush, having a multiplicity of bristles which capture urine and release it back when in contact with the liquid transfer member.

In addition to a sample-absorbing member, the urine collection member may include an integral collection cup, splash guards or a measuring systems to ensure that sufficient sample volume is collected. For example, by raising the rim of the housing surrounding the absorbent pad above the surface of the absorbent pad, an integral collection cup is created in which a volume of urine can be captured prior to absorption into the absorbent pad.

The present invention provides a simple-to-use, one piece device for testing for an analyte in a liquid sample. Because the device can be supplied in the folded condition, the size of the device during shipping and at point-of-sale can be relatively small, while at the same time providing a long device which will minimize risk of contact with urine or other liquid samples when holding the opposite end of the device. Furthermore, the used sample collection member is enclosed within the folded device, thus reducing the likelihood of inadvertent contact with urine or other sample liquids.

CLAIMS

1. Device for detection of a target substance in a liquid sample comprising:

(a) an first housing member (10) having a pivot end and a free end;

(b) a second housing member (11) having a pivot end and a free end, said pivot end of the second housing member (11) being pivotably connected to the pivot end of the first housing member (10), and said first and second housing members (10, 11) being movable between an open position in which the first and second housing members (10,11) are disposed substantially linearly, and a folded position in which the free end of the first housing member (10) and the free end of the second housing member (11) are disposed in proximity to one another;

(c) a sample-absorbing member (15) disposed at the free end of first housing member (10); and

(d) a chromatographic test element (45, 48) responsive to the target substance disposed on second housing member (11), wherein sample liquid collected in the sample-absorbing member (15) is transferred to the chromatographic test strip when the device is in the folded position but not when the device is in the open position.

2. A device according to claim 1, further comprising a liquid transfer member (44) disposed on the second housing member (11) in contact with the chromatographic test element (45, 48), said liquid transfer member (44) making contact with the sample-absorbing member (15) when the device is in the folded position.

3. A device according to claim 2, further comprising an upstream absorbent pad (46) disposed in contact with the chromatographic test element (45) for drawing liquid through the chromatographic test element (45) from the sample-absorbing member (15).

4. A device according to any of claims 1 to 3, wherein the chromatographic test element comprises a reagent pad (48) containing a first antibody specific for a first epitope of the target substance and a chromatographic test strip (45) having

formed thereon a test region comprising a second antibody specific for a second epitope of the target substance and a control region which binds to the first antibody in the presence or absence of the target substance.

5. A device according to any of claim 1 to 4, wherein the target substance is human chorionic gonadotropin.

6. A device according to any of claims 1 to 5, wherein the first housing member (10) is received within the second housing member (11) in the folded position.

7. A method for detection of a target substance in a liquid sample, comprising the steps of applying the sample to the sample absorbing member of a device according to any of claims 1 to 6, and evaluating the chromatographic test element.

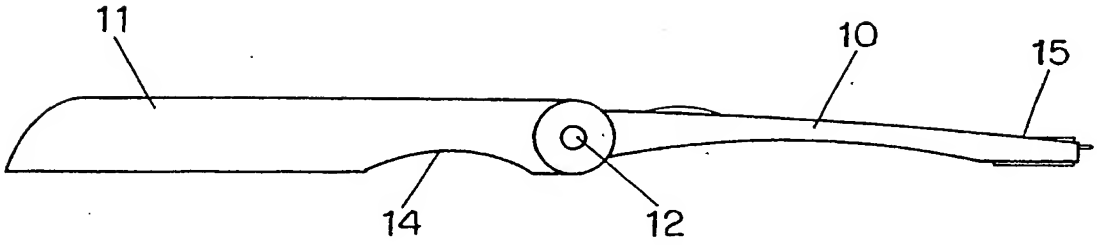

FIG. 1

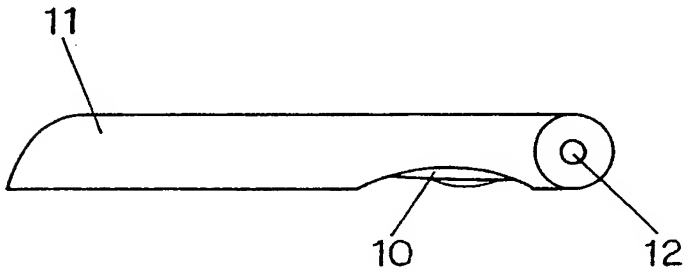

FIG. 2

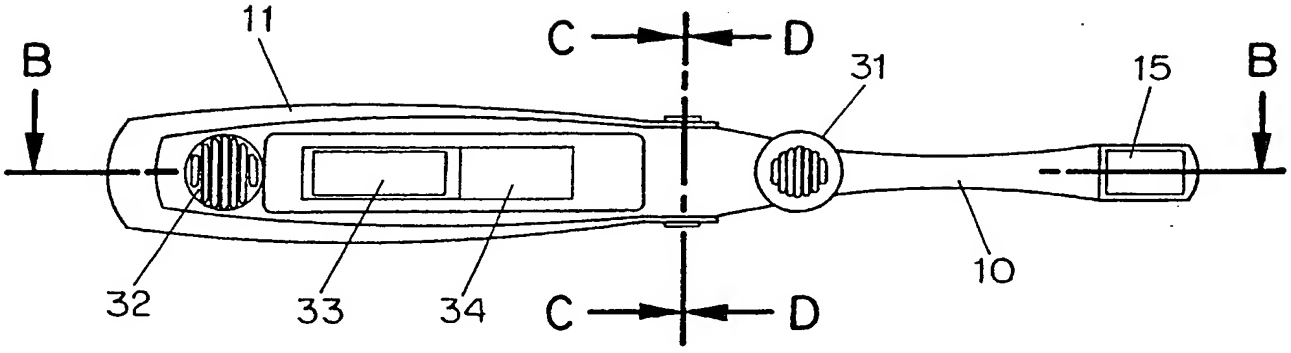

FIG. 3

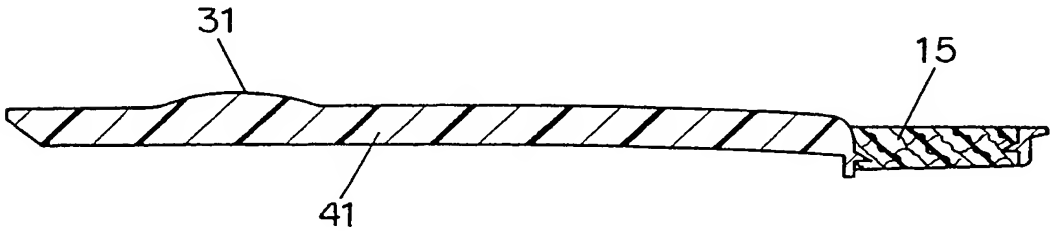

FIG. 4A

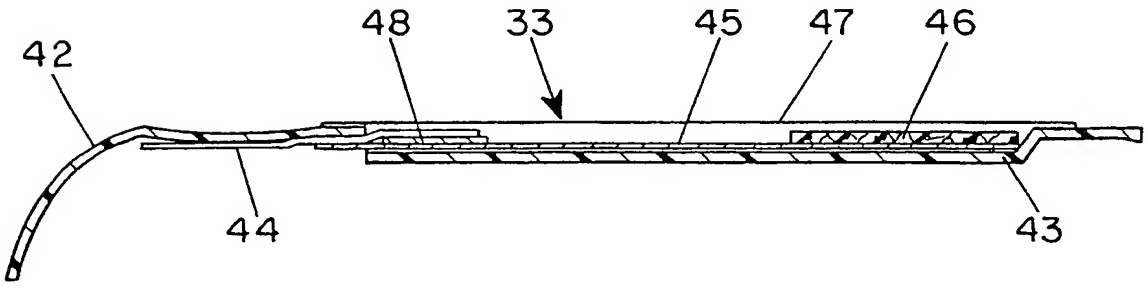

FIG. 4B

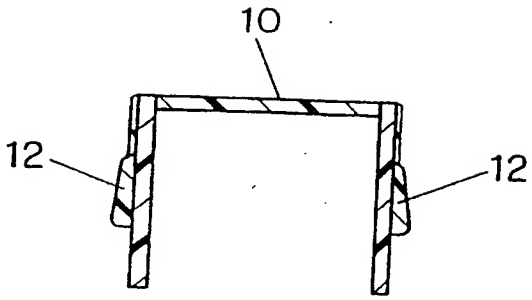

FIG. 5A

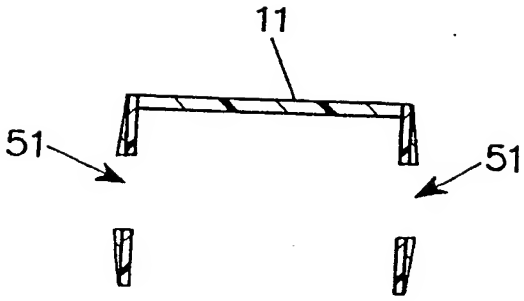

FIG. 5B

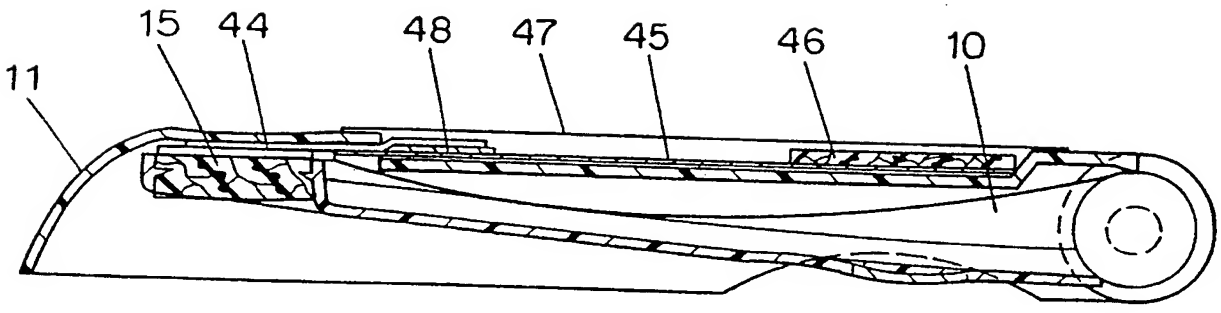

FIG. 6

INTERNATIONAL SEARCH REPORT

Inter .tional Application No
PCT/US 98/08393

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 G01N33/68 G01N33/543 G01N33/76

According to International Patent Classification(IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 95 08761 A (POLYFILTRONICS INCORPORATED) 30 March 1995 see page 7, line 16 - line 18; figures 12,13 see page 10, line 19 - page 11, line 8 see page 12, line 24 - page 13, line 6 ---	1-7
Y	PATENT ABSTRACTS OF JAPAN vol. 95, no. 8, 29 September 1995 & JP 07 120467 A (DAINIPPON PRINTING COMPANY) cited in the application see abstract ---	1-7
A	EP 0 291 194 A (UNILEVER N.V.) 17 November 1988 cited in the application see the whole document --- -/--	1-7

[X] Further documents are listed in the continuation of box C.

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	J.T. HANLON ET AL.: "An evaluation of the sensitivity of five home pregnancy tests to known concentrations of human chorionic gonadotropin." AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY, vol. 144, no. 1, 1982, pages 778-782, XP002073204 st. louis mi usa see the whole document	1-7

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inte...ational Application No
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